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RUSSELL R. BURTON

CREW SYSTEMS DIRECTORATE ARMSTRONG LABORATORY BROOKS AIR FORCE BASE, TEXAS

### Iheoretical Considerations:

Clearly, physiologic adaptation to terrestrial life for all animals is assured only by frequent encounters with gravity. Indeed, upon exposure to weightlessness in space flight, losses of physiologic functions quickly begin. Some physiologic parameters change more rapidly than others, but the deconditioning process starts rapidly.

The rates of functional losses for all affected parameters are interesting in that they appear to approach a limit; i.e., losses of these functions may not continue until indefinitely. The regulation of this functional asymptotic response to space is not known, but probably based on functional requirements of the body to life itself and perhaps genetic expression. The latter controlling mechanism (DNA) functions only on aquatic (weightless) animals on Earth -- land animals must stimulate these physiologic functions as they relate to gravity on a regular frequent basis.

This loss of regulation upon entering the weightless environment is fascinating since land-based animals including the humans have evolved from millions (perhaps billions) of years of terrestrially adapted ancestors. One would expect some DNA involvement in the regulation of its physiology, but it appears to be absent. Therefore, if the functional debilitation of space is to be denied, we must begin to understand the adaptation process of the sole basis for the control of our physiologic processes on land; i.e., how gravity regulates our biologic functions. To learn about this regulatory mechanism, some inquiry into how aquatic animals first adapted to living on land might be helpful.

Little is known how aquatic animals adapted to living on land experiencing for the first time the force of gravity as it constantly tugged at the body. Moving from the weightlessness of a water environment to 1g must have been physiologically very stressful to these animals. Certainly, this experience must be similar to that of animals exposed to G levels that are greater than 1g. These types of G exposures have been studied extensively on animals. Consistently, the results show that these animals become stressed eventually, relieving the stressful state by physiologically adapting to the increased G environment (6).

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Several adaptates have been identified that help develop this adaptation. Anatomical and physiologic adaptates include: (a) muscles, (b) exercise capacity, (c) body mass, (d) nutritional requirements, (e) plasma volume, and (f) red blood cell mass (5, 8, 9, 10, 16, 17, 18, 19). These adaptates are identical to those that change with extended exposures to weightlessness in space. These similarities provide substantial evidence that the body responses to change in G or gravity are qualitatively identical (20, 21). The quantitative nature of these changes appropriately follows the physical forces involved; i.e., affected parameters change in concert with an increase or decrease in the G/g forces.

So be it that as these aquatic animals, genetically adapted to the weightlessness of the water environment, moved onto land, physiologic stress occurred and in response adaptates were developed. By nature, stress is uncomfortable, even painful, so that these animals would escape the stress by returning to the water. There can be little doubt that adaptation to gravity occurred with regular periodic exposures to its physical force (6,11).

We may also assume that regular exposures occurred on a daily basis and at about the same time, when animals are most active, since biorhymicity has a significant influence on the activities of all animals; it is likely this gravity exposure occurred in the middle of the day during peak-activity periods. It is reasonable therefore to believe that circadian rhythms will play a role in the response of the body to periodic exposure to gravity or G. This relationship is important to consider if and when gravity is substituted periodically by G on a regular basis in space to prevent physiologic deconditioning.

As these aquatically adapted animals moved onto the land, all physiologic functions were affected similarly, but it was probably the bones and muscles that were most abused by gravity. Although functional in water, their role was changed directly from singularly one of motion to an additional role of support against gravity. For the first time, extensors had a primary role to perform on land besides loading the flexors in their motion role in water. The fatigue that developed within these specific groups of muscles must have been substantial, limiting their daily exposure duration to land living. It is for this reason that exercise in space is not completely effective in preventing a decline in its functional capability, specifically its major role in support of the body against gravity.

The cardiovascular system was also challenged in support of terrestrial living. Cardiovascular stimulation by gravity is provided by the intravascular hydrostatic pressures that develop immediately upon exposure to it. A sudden increase in hydrostatic pressure within the vascular system in response to land habitation (i.e., hydrostatic pressure is directly related to column height because of G or g) had profound effects on arterial and venous blood pressure, flow, and volume, perhaps even red blood cell mass. This effect too then limited exposure to moving on land as blood constituent fluids rapidly leaked extravascularly.

<sup>1</sup>G represents the inertial force that develops in response to acceleration. G has been shown to be physically identical to gravity by Einstein and Mach in their Theory of Equivalence (Smith 15).

As animals became larger, the role of gravity on intravascular hydrostatic pressure related blood pressure (particularly blood column height) became more important.

More recently over the last several thousand years, bipedal posture of the human has placed an additional burden on the cardiovascular system in support of orthostasis and now even more recently with the advent of rockets and airplanes, increased G tolerance. The baroceptors were recruited by the body to perform this task. These clever regulators were perfect for the job since they were already regulating blood pressure in the brain to prevent cerebral hypertension. Adaptation in support of orthostasis by these baraceptors was not necessary as evidenced by arterial blood pressure responses of quadripeds to increased G (3). Lower body negative pressure (LBNP) used in space in support of the cardiovascular system does not directly affect the intravascular hydrostatic pressures. Its very slow, indirect effects are a poor substitute for the direct profound effects of gravity.

The role of gravity in the maintenance of other physiologic functions is less clear (perhaps less direct), but measurement in space suggests that others may indeed prevail; e.g., the immune system. Much greater questions arise. Can terrestrially adapted animals remain healthy in a weightless environment indefinitely without gravitational stimulation? Once adaptation to the space environment has been completed (perhaps after several years), can readaptation (back to) Earth's gravity occur?

Until we know these answers, there is no substitute for gravity except, of course, the inertial forces of acceleration that is provided by centrifugation (1, 2, 4, 7, 13 14). The application of gravity or G in its regulatory role in physiology is not well understood. Increased G animal studies have been helpful in this regard (8). But limitations are evident in its application in the maintenance of physiologic function to reduced gravitational forces. Increased G studies have identified those physiologic functions at greatest risk in space. These studies have even identified successful processes of G application that are useful in stimulating its adaptation process; periodic daily exposures to increased G were effective in adapting animals to continuous exposure to increased G environments (11). Physiologic regulatory processes are stimulated by periodic exposures to increased G, probably recapitulating the same adaptive processes that occurred when animals moved onto the land. And as with frequent exposures to increased G, frequent exposures to gravity maintains that adaptation.

The time requirements of daily exposure to increased G or gravity to maintain that adaptation is not known. Nor is the role of the intensity of this G stimulation on this adaptation process understood. Can these gravity based regulatory processes be stimulated more rapidly by G levels greater than 1g? Certainly this question is profound and intrinsic in understanding the bases of gravitation regulation of physiologic processes.

It is well known that the general nature of loss of physiologic regulation in weightlessness begins rapidly and continues unabated for an undetermined period of time. This loss of regulation can be interrupted with various stimulations (some better than others) and most effectively when regularly applied (Figure 1). Consistently, regu-

latory phenomena respond to the active process of a useful stimulation more rapidly than the passivity of its decay in the absence of that stimulation (Figure 2) (12).

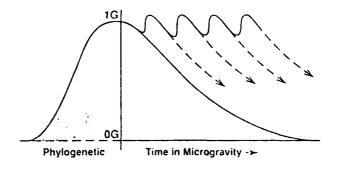


FIGURE 1: Theoretical response of physiologic function in a microgravity environment. Even though adaptation to terrestrial habitation has developed for millions of years ("phylogenetically"), that functional adaptation begins to fade rapidly upon the loss of gravity. Repeated regular stimulation by G may prevent its decay.

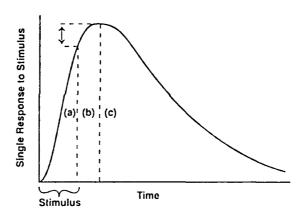


FIGURE 2: Physiologic functions respond to active stimulation (a) more rapidly than the passive nature of the loss of function (c). Functional stimulation continues (b) even after the stimulant has been removed.

It may also be assumed that the stimulation that is most similar to the requirements of the regulatory process is the most effective; i.e., G is a better stimulation for gravitational regulation than LBNP, exercise, or bungey cords. Clearly, then the importance of the role of G in preventing deconditioning of microgravity must be thoroughly ascertained for long-term space voyages.

But perhaps the stimulatory role of gravity can be hastened by applying more of it at one time (Figure 3). These conditions can be met with increased G (centrifugation). The human is rather tolerant to increased G, although duration of exposure is limiting at 2G and above. At higher levels, exposure duration rapidly reduces G tolerance exponentially (8).

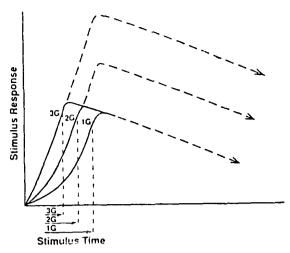


FIGURE 3: Theoretically, the stimulation of higher levels of G may be more effective, requiring less time than lower levels.

The nature of this relationship between G-level and G-duration as they interact on physiologic processes is shown in Figure 4. Three zones of gravitational stimulation are identified where G exposures are: (a) insufficient, (b) adequate, and (c) over-stimulation resulting in unregulated physiologic stress. At this time, these zones have not been quantified nor even identified. The basis of physiologic regulation by gravity will not be understood until these zones of adaptation are established. The identification of the quantitative nature of these zones are also important to operations, to wit: (a) Are the higher G levels tolerable for sufficient durations by humans to be effective? (b) Do the lower G levels require exposure durations short enough to be useful in preventing physiologic deconditioning in space?

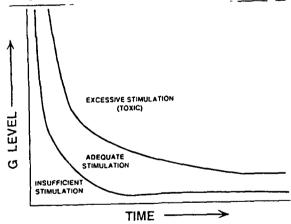


FIGURE 4: G x time exposure requirements to prevent physiologic deconditioning during stays in microgravity.

## Recent Relevant Research Results:

Recent weightless simulation studies have supported this concept of periodic increased G exposures to prevent space deconditioning. Shulzhenko and Vil-Viliams (14) using 3-day dry immersion simulation of weightlessness measured human tolerance to 3G. Three days of immersion reduced 3G tolerance by 21%, but approximately 2 hrs of daily 1.2G, 1.6G or 1.9G with immersion showed less reductions in G tolerance of only 18%, 7% and 1% respectively. Their conclusion is irrefutable that

increased G exposures is useful and higher G levels are most beneficial. Relating those data of Shulzhenko and Vil-Viliams (14) to the (G x Time) concept identified in Figure 4, the daily exposure period of time required to prevent any loss of tolerance to 3G is 245 min of 1G, but only 82 min of 3G (Figure 5).

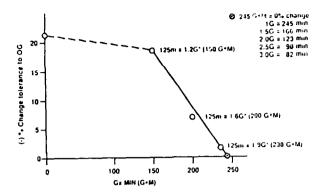


FIGURE 5: Using data from Schulzenko and Vil-Viliams (14), 4 hrs at 1G is required to maintain 3G tolerance while inhabiting microgravity, but only 82 mi at 3G is required.

More recently, Vernikos and Ludwig (22) reported on a 4-day -6% head down bedrest with controls (no standing nor exercise exposure) and 4 groups of the same 9 males each with daily periodic 2 or 4 hr exposures to standing or walking at 1g. Periodic daily exposures to 1g were useful in preventing decreases in peak Vo<sub>2</sub>, plasma volume, and orthostatic tolerance and increases in urinary calcium. Interestingly and quite unexpectedly, longer 1g periodic exposure periods were not always most beneficial nor was the inclusion of exercise (Table 1).

Earlier research in our laboratory (7) clearly showed that a short-radius centrifuge of 5 ft (1.5 m) radius was easily tolerated by humans in a flexed-leg position up to 7G (76 rpm). Also that with the subject's head only 26 in (66 cm) from the centrifuge center, beneficial cardiovascular effects of the increased intravascular hydrostatic pressures from the increased G were provided. Simply, this short-radius centrifuge produced G that would be effective in stimulating the cardiovascular system in space.

TABLE I: Effectiveness in preventing physiologic responses to 4 days of -6% head down bedrest. S2 and S4 denotes subjects Standing 2 or 4 hrs daily. W2 and W4 identifies Walking 2 or 4 hrs daily (22).

		S2	S4	W2	W4
Orthostatic Intolerance		++	+++	+	٥
Peak VO2		•	**	***	•••
Plasm	na Volume	o	+++	٥	•••
	ry Calcium retion (4 Day)	0	0	+++	***
***	Most Effective				
++	Effective				
+	Partially Effective				
0	Not Effective				

## \*Operational Concerns:

Using regular daily exposures of increased G to prevent physiologic deconditioning during stays in microgravity will require considerable research to determine if the concept is useful and the optimum G exposure schedules. In addition, the role of biorhymicity interaction with gravity in physiologic regulation and the interaction of numerous other "treatments" with periodic G exposure to prevent physiologic deconditioning in microgravity will have to be determined (Figure 6).

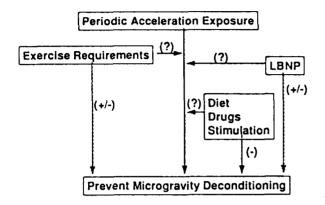


FIGURE 6: The relationships of exercise, lower body negative pressure (LBNP), diet, drugs, and electrical stimulation with periodic G exposure to prevent microgravity physiologic deconditioning is unknown.

#### Conclusion:

The role of G in space using a short-radius centrifuge has operation implications in preventing physiologic deconditioning from weightlessness. The relationship between periodic gravity exposures on simulated weightless effects, once determined systematically, will provide crucial information on the role of gravity as a regulator of physiologic functions.

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